Clinical trial results:
A comparison of the effectiveness of prostaglandin gel and tablet preparations in induction of labour at term.

Summary

EudraCT number	2004-003797-28
Trial protocol	GB
Global end of trial date	01 November 2006

Results information

Result version number	v1 (current)
This version publication date	30 May 2020
First version publication date	30 May 2020

Trial information

Trial identification

Sponsor protocol code	EDMK4002

Additional study identifiers

ISRCTN number	ISRCTN70152691
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College Healthcare NHS Trust
Sponsor organisation address	Research Office, Room 221, Medical School Building, St Mary's, London, United Kingdom, W2 1PG
Public contact	Douglas Keith Edmonds, Imperial College Healthcare NHS Trust, k.edmonds@imperial.ac.uk
Scientific contact	Douglas Keith Edmonds, Imperial College Healthcare NHS Trust , k.edmonds@imperial.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 November 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 November 2006
Global end of trial reached?	Yes
Global end of trial date	01 November 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether Prostaglandin Gel is more effective in term induction of labour than Prostaglandin Tablets. The main outcome measure will be time between the start of the induction process and delivery of the baby.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2004
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 165
Worldwide total number of subjects	165
EEA total number of subjects	165

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	165
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Women undergoing induction of labour with a cephalic presentation (singleton) or first twin cephalic at term (from ≥36+6 to 42 weeks of gestation) were recruited.

Pre-assignment

Screening details:

251 eligible women were approached, of whom 218 (86.8%) provided initial written consent. Of these, 172 (68.52%) were admitted for induction of labour. Following reconfirmation of consent, seven of those 172 (4%) declined.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Prostin E2 gel

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Prostin E2 gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Vaginal use

Dosage and administration details:

The gel contains 1 or 2 mg of dinopristone in 3 grams of thick clear gel in sterile opaque syringes. Prior to the administration of the study drug a fetal cardiogram was performed for 20 minutes. Provided that the fetal heart rate pattern was within normal limits the trial coordinator performed a vaginal examination, recorded the initial Bishop score, and administered gel into the posterior vaginal fornix. The fetal cardiogram was then continued for a further 60 minutes. In patients randomised to receive dinopristone gel, a nulliparous woman with an unfavourable cervix (i.e. with a modified Bishop score ≤ 4) was given an initial dose of 2 mg. Multiparaous women and nulliparous women with a favourable cervix (i.e. with a modified Bishop score of 5–7) were administered an initial dose of 1 mg. Two further vaginal examinations were then performed at intervals of 6 hours, at which a further 1 mg of gel was administered until the cervix became favourable (Bishop score ≥ 8).

Arm title	Prostin E2 tablets

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Prostin E2 tablets
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Vaginal use

Dosage and administration details:

Prior to the administration of the study drug a fetal cardiogram was performed for 20 minutes. Provided that the fetal heart rate pattern was within normal limits the trial coordinator performed a vaginal examination, recorded the initial Bishop score, and administered dinopristone tablets, 3 mg was administered into the posterior vaginal fornix. The fetal cardiogram was then continued for a further 60 minutes. Two further vaginal examinations were then performed at intervals of 6 hours, at which a further 3mg tablet was administered until the cervix was favourable (Bishop score ≥ 8).

Number of subjects in period 1[1]	Prostin E2 gel	Prostin E2 tablets
Started	81	82
Completed	81	82

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial as there was only data available for a certain number of participants.

Baseline characteristics

Reporting groups	
Reporting group title	Prostin E2 gel
Reporting group description: -	
Reporting group title	Prostin E2 tablets
Reporting group description: -	

Reporting group values	Prostin E2 gel	Prostin E2 tablets	Total
Number of subjects	81	82	163
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	32.5	33	
inter-quartile range (Q1-Q3)	26 to 37.40	29 to 37	-
Gender categorical Units: Subjects			
Female	81	82	163
Male	0	0	0
Indication for labour induction: postdate Units: Subjects			
postdate	41	51	92
not postdate	40	31	71
Initial Bishop score Units: Subjects			
0-3	60	58	118
>3	21	24	45
Median gestation (IQR) days Units: days			
median	284	288	
inter-quartile range (Q1-Q3)	274 to 290	276 to 290	-

End points

End points reporting groups

Reporting group title	Prostin E2 gel
Reporting group description: -	
Reporting group title	Prostin E2 tablets
Reporting group description: -	

Primary: Median (IQR) interval from induction to delivery (minutes)

End point title	Median (IQR) interval from induction to delivery (minutes)[1]
End point description:	
End point type	Primary
End point timeframe:	
Induction to delivery	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Comparisons between continuous variables by study drug formulation and by parity used the Mann–Whitney Utest. The Kruskal–Wallis test with Bonferroni correction was used to compare the interval from induction of labour to delivery by Bishop score. Univariate comparisons of dichotomous data were performed with the use of the chisquare (Fisher's exact) test. The P values for all hypothesis tests were twosided, and P values of 0.05 or less were considered to indicate statistical significance.

End point values	Prostin E2 gel	Prostin E2 tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	82		
Units: minutes				
median (inter-quartile range (Q1-Q3))	1400 (690 to 2280)	1780 (960 to 2640)		

Statistical analyses

No statistical analyses for this end point

Primary: Median (IQR) interval from induction to delivery (minutes)-primiparous

End point title	Median (IQR) interval from induction to delivery (minutes)-primiparous[2]
End point description:	
End point type	Primary
End point timeframe:	
Induction to delivery	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Comparisons between continuous variables by study drug formulation and by parity used

the Mann–Whitney Utest. The Kruskal–Wallis test with Bonferroni correction was used to compare the interval from induction of labour to delivery by Bishop score. Univariate comparisons of dichotomous data were performed with the use of the chisquare (Fisher's exact) test. The P values for all hypothesis tests were twosided, and P values of 0.05 or less were considered to indicate statistical significance.

End point values	Prostin E2 gel	Prostin E2 tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	82		
Units: minutes				
median (inter-quartile range (Q1-Q3))	1560 (1020 to 2310)	2160 (1170 to 2760)		

Statistical analyses

No statistical analyses for this end point

Primary: Median (IQR) interval from induction to delivery (minutes)-multiparous

End point title	Median (IQR) interval from induction to delivery (minutes)-multiparous[3]

End point description:

End point type	Primary

End point timeframe:

Induction to delivery

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Comparisons between continuous variables by study drug formulation and by parity used the Mann–Whitney Utest. The Kruskal–Wallis test with Bonferroni correction was used to compare the interval from induction of labour to delivery by Bishop score. Univariate comparisons of dichotomous data were performed with the use of the chisquare (Fisher's exact) test. The P values for all hypothesis tests were twosided, and P values of 0.05 or less were considered to indicate statistical significance.

End point values	Prostin E2 gel	Prostin E2 tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	82		
Units: minutes				
median (inter-quartile range (Q1-Q3))	960 (655 to 2100)	1350 (780 to 2460)		

Statistical analyses

No statistical analyses for this end point

Primary: Failed induction

End point title	Failed induction[4]

End point description:

End point type	Primary

End point timeframe:

Induction to delivery

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Comparisons between continuous variables by study drug formulation and by parity used the Mann–Whitney Utest. The Kruskal–Wallis test with Bonferroni correction was used to compare the interval from induction of labour to delivery by Bishop score. Univariate comparisons of dichotomous data were performed with the use of the chisquare (Fisher's exact) test. The P values for all hypothesis tests were twosided, and P values of 0.05 or less were considered to indicate statistical significance.

End point values	Prostin E2 gel	Prostin E2 tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	82		
Units: Number of patients	1	9		

Statistical analyses

No statistical analyses for this end point

Primary: Failed induction in primiparous mother

End point title	Failed induction in primiparous mother[5]

End point description:

End point type	Primary

End point timeframe:

Induction to delivery

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Comparisons between continuous variables by study drug formulation and by parity used the Mann–Whitney Utest. The Kruskal–Wallis test with Bonferroni correction was used to compare the interval from induction of labour to delivery by Bishop score. Univariate comparisons of dichotomous data were performed with the use of the chisquare (Fisher's exact) test. The P values for all hypothesis tests were twosided, and P values of 0.05 or less were considered to indicate statistical significance.

End point values	Prostin E2 gel	Prostin E2 tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	82		
Units: Number of patients	1	8		

Statistical analyses

No statistical analyses for this end point

Primary: Failed induction in multiparous mother

End point title	Failed induction in multiparous mother[6]

End point description:

End point type	Primary

End point timeframe:

Induction to delivery

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Comparisons between continuous variables by study drug formulation and by parity used the Mann–Whitney Utest. The Kruskal–Wallis test with Bonferroni correction was used to compare the interval from induction of labour to delivery by Bishop score. Univariate comparisons of dichotomous data were performed with the use of the chisquare (Fisher's exact) test. The P values for all hypothesis tests were twosided, and P values of 0.05 or less were considered to indicate statistical significance.

End point values	Prostin E2 gel	Prostin E2 tablets		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	82		
Units: Number of patients	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: During study	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Frequency threshold for reporting non-serious adverse events: 5 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No adverse events detailed in the publication, https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/j.1471-0528.2011.02901.x, in BJOG and International Journal of Obstetrics and Gynaecology

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/21429067